

## **REMARKS**

Reconsideration and withdrawal of the rejections set forth in the Office Action dated June 14, 2006 are respectfully requested. A separate petition for a one-month extension of time accompanies this amendment.

### **I. Amendments**

The specification is amended to correct typographical errors and to capitalize all references to trademarks.

Claims 9, 13, and 18 are amended to recite the chemical names for the series of surfactants identified by the trade designation TWEEN®, and for the specific surfactants known as TWEEN® 20 and TWEEN® 80. Because chemical names are synonymous with the surfactant product, the amendment does not introduce new matter.

Claims 11 and 20 are amended to recite the chemical names for the series of surfactants referred to as PLURONIC®. Because chemical names are synonymous with the surfactant product, the amendment does not introduce new matter.

Claims 14 and 23 are amended to omit reference to the viscosity of the coating formulation.

### **II. Rejections under 35 U.S.C. § 112, second paragraph**

Claims 9, 11, 13, 18, and 20 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, claims 9, 11, 13, 18, and 20 were found to be vague and indefinite because of improper use of a trademark.

As noted above, claims 9, 13, and 18 are amended to recite the chemical names for the surfactants TWEEN® 20 and TWEEN® 80. For the Examiner's convenience, applicants submit herewith (i) a material safety data sheet for TWEEN® 20, showing the chemical name. Applicants also submit herewith (ii) a technical article showing that TWEEN® 80 is synonymous with Polysorbate 80, and (iii) a material safety data sheet for Polysorbate 80 showing its chemical name.

Claims 11 and 20 are amended to recite the chemical name for the surfactants designated by the tradename PLURONIC®, which are block copolymers of ethylene oxide and propylene oxide. For the Examiner's convenience, applicants submit (iv) a product information page on the PLURONIC® surfactants indicating this fact.

In view of these amendments, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

### **III. Rejections under 35 U.S.C. § 103**

Claims 1-3, 5-7, 12, 15-16, and 21 were rejected under 35 U.S.C. §103 as being obvious over Trimmer *et al.*, WO 96/10630 ("Trimmer").

Claims 8-10, 13, 17-19, and 22 were rejected under 35 U.S.C. §103 as being obvious over Trimmer in view of Baum, U.S. Patent No. 6,294,515.

Claim 4 was rejected under 35 U.S.C. §103 as being obvious over Trimmer in view of Heinz *et al.*, U.S. Publication No. 2002/0012741 ("Heinz").

Claims 11, 14, 20, and 23 were rejected under 35 U.S.C. §103 as being obvious over Trimmer in view of Jain *et al.*, U.S. Patent No. 4,505,890 ("Jain").

These rejections are respectfully traversed for the following reasons.

#### **A. The Present Claims**

The present claims relate to a method of coating the surface of one or more microprojections of a microprojection array comprising the steps of:

(i) providing a microprojection array comprised of one or more microprojections; (ii) treating the surface of one or more of said microprojections of the microprojection array with a method selected from group consisting of chemical pre-etching, plasma treatment, heat treating, rinsing with an alkaline detergent and rinsing with a wetting agent; (iii) providing a coating formulation comprising an active agent; (iv) applying the coating formulation to the treated surfaces of the one or more microprojections; and (v) drying the coating formulation onto the surfaces to form a coating.

B. The Applied Art

TRIMMER describes a method for introducing an agent into a cell. The method involves piercing the cell with microbarbs that contain the agent.

BAUM discloses a low-foaming rinse agent based on sorbitol.

HEINZ describes a method to apply a lubricant to the interior wall of a container, where the lubricant is irradiated with infrared radiation to attach the lubricant to the container wall.

JAIN discloses an oral table for controlled release of a drug, where the table can be coated with a mixture of celluloses (Col. 6, lines 27-31).

C1. Analysis: Rejection over Trimmer

Prior to analyzing the rejection over Trimmer, Applicants wish to correct the Examiner's characterization of the claimed method. In the June 14, 2006 Office action, on page 4 the Examiner summarizes Applicants' claim incorrectly. The Examiner has mischaracterized the claim in stating that the step of treating the surface of one or more microprojections is *after* drying the coating. This is clearly not the case, since step (ii) of applicants' claim recites, "applying said coating formulation to said treated surfaces of said one or more microprojections" (emphasis added). Thus, the applying step is subsequent to the treating step.

Also prior to analyzing the rejection over Trimmer, Applicants wish to point out that in Example 1 of Trimmer, fabrication of microprobes from a silicon wafer is described (as correctly stated by the Examiner on page 5 of the June 14, 2006 Office action). The steps of cleaning, heating, and etching that are noted and emphasized by the Examiner are directed to *formation* of the microprobes on a silicon wafer. Based on the emphasis applied to these steps by the Examiner in the Office action, it appears that the Examiner likens these formation steps to the claimed step of *treating* the surface of one or more of said microprojections. Since microprojections are not formed until the etching process is complete, there are no microprojections present to be subjected to a treating step. Thus, these formation steps cannot be considered to be "treating the surfaces of microprojections".

Turning now to the analysis of the rejection based on Trimmer, the legal standard for obviousness requires that three basic criteria be met (M.P.E.P. § 2143).

The third criterion is that the prior art references (or references when combined) must teach or suggest all the claim limitations.

The method set forth in the present claims includes the feature of treating the surface of one or more microprojections. As mentioned above, this step is conducted prior to applying a coating formulation to the surfaces. The treating methods are selected from chemical pre-etching, plasma treatment, heat treating, rinsing with an alkaline detergent, and rinsing with a wetting agent.

In Example 1 of Trimmer, fabrication of microprobes from a silicon wafer is described. Nothing in this example relates to “treating” the surfaces of microprobes, but instead relates to fabrication of microprobes. Thus, this teaching cannot be considered to be a step of “treating” the surface of the microprobes, since the microprobes are not present until the etching is complete.

In Example 2 of Trimmer, the microprobes are described as being soaked in 95% ethanol for 20-30 minutes and then washed three times with water (page 16, lines 34-36). This step is not one of the treating methods recited in applicants’ claims. Specifically, soaking microprobes formed on a silicon wafer in ethanol and rinsing with water is not a chemical pre-etching since ethanol soaking and water rinsing will not form pits in the silicon. (Note that on page 8, in paragraph [00019] of applicants’ specification the chemical pre-etching treatment is described as “formation of pits by chemical pre-etching”). Nor is the ethanol soak/water rinse of Trimmer a plasma treatment, heat treatment, an alkaline detergent rinse, or a rinse with a wetting agent.

Accordingly, applicants’ submit that the teaching in Trimmer does not teach or suggest all the claim limitations. Therefore, a prima facie case of obviousness has not been established. Withdrawal of the rejection under 35 U.S.C. §103 based on Trimmer is respectfully requested.

## C2. Analysis: Rejection over Trimmer in view of Baum

Dependent claims 8-10, 13, 17-19 and 22, which relate to the embodiment of treating the microprojection surfaces with a wetting agent such as a surfactant. It is the Examiner’s position that it would be obvious to apply the teaching of the low-foaming, sorbitol based surfactants of Baum, designed to prevent spotting and streaking of

dishes in a dishwashing machine, to the teachings of Trimmer of a wetting agent included in a drug solution.

The legal standard for obviousness requires that the combined teachings of the prior art references teach or suggest all the claim limitations (M.P.E.P. § 2143). The combination of Trimmer and Baum fails to satisfy this requirement. Trimmer does not teach "treating" the surfaces of the microprojections, for the reasons given in C1 above.

Moreover, Baum does not satisfy this deficiency, since the rinse agents for dishes described in Baum may or may not be relevant for treating the surface of a material before application a drug coating formulation. Since neither Baum nor Trimmer teach treating the surface with a wetting agent, followed by applying a coating formulation to the treated surface, the combination does not teach or suggest all of the claim features.

Furthermore, the suggestion of the Examiner to include the rinse agents of Baum to the drug coating solution of Trimmer does not even capture the steps of applicants' claim. In the instant claims, a wetting agent is used to treat the surfaces of the microprojections prior to applying a drug coating solution, rather than including a wetting agent in the drug formulation.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

### C3. Analysis: Rejection over Trimmer in view of Heinz

Claim 4, rejected based on the combined teachings of Trimmer with Heinz, relates to the embodiment where the treating step comprises plasma treating. It is the Examiner's position that it would be obvious to use a plasma treatment, mentioned by Heinz, as a pre-conditioning step for the microprobes of Trimmer, since Trimmer teaches several pre-conditioning steps.

In fact, the only pre-conditioning step taught by Trimmer is to soak the microprobes in ethanol and then rinse with water. As mentioned above, the other steps noted by the Examiner of cleaning, heating, and etching are not pre-conditioning, but formation of microprobes.

It would not be obvious to modify Trimmer to utilize a plasma treatment method as a microprobe pre-conditioning step based on the teaching in Heinz. The step of

soaking microprobes in ethanol and rinsing with water is a cleaning step to remove surface impurities. In contrast, plasma treatment will result in etching of a surface or deposition of a material on a surface. Nothing in Trimmer suggests such a step prior to coating the microprobes. The mere mention in Heinz that plasma treatment is a conventional step of pre-conditioning is in the context of applying a silicone coating to plastic syringes. This mention does not guide one to apply plasma treatment to the microprobes of Trimmer in place of an ethanol soak followed by a water rinse, particularly since Trimmer has nothing to do with applying silicone to a plastic surface.

Thus, the rejection based on the combination of Trimmer and Heinz suffers from a failure of the combined teachings to show or suggest all of the claim limitations. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

**C4. Analysis: Rejection over Trimmer in view of Jain**

The Examiner asserts it would be obvious to take the teaching in Jain of a HPMC coating of an oral tablet and apply the HPMC as a wetting agent in the drug solution of Trimmer. This rejection is misplaced for the reasons given in C2 above, and primarily because this combination, as put forth by the Examiner, does not show or suggest the present claims. Applicants' claims recite treating the surface of the microprojections with, for example, a wetting agent, and then applying a drug coating formulation the treated surfaces. The Examiner's line of reasoning suggests putting the wetting agent, HPMC, into a drug solution, which is not what the present claims recite

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

**IV. Double-Patenting Rejections**

Claims 1-3, 5-7, and 15-16 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,855,372 ("372 patent") in view of Trimmer.

Claims 1-3 and 15-16 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-30 of co-pending application serial no. 10/674,626 ("the '626 application").

These rejections are traversed for the following reasons.

A. Legal Standard

According to M.P.E.P. 804(ii)(B)(1), in determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent?

B. Analysis: Rejection Based on the '372 patent combined with Trimmer

Claims 1-12 of the '372 patent relate to a method for coating a liquid onto microprojections. None of the claims include a step of "treating the surface of one or more of said microprojections of said microprojection array with a method selected from group consisting of chemical pre-etching, plasma treatment, heat treating, rinsing with an alkaline detergent and rinsing with a wetting agent", as presently claimed.

Nor does Trimmer teach this step, for all the reasons given in III above. Specifically, Trimmer fails to show or suggest treating the surface of a microprobe by chemical pre-etching, plasma treatment, heat treatment, an alkaline detergent rinse, or a rinse with a wetting agent.

Thus, the present claims are not merely an obvious variation of the claims in the '372 patent in view of Trimmer, since one of the claims steps is not taught. Therefore, withdrawal of the rejection for obviousness-type double patenting is respectfully requested.

C. Analysis: Rejection Based on the '626 application combined with Trimmer

The Examiner asserts that claims 29-30 of the '626 application teach etching microprojections and then coating them with a drug solution. Applicants respectfully note that the step in claims 29-30 of the '626 application related to "etching" occurs prior to formation of the microprojections and cannot be considered a step of "treating the surface(s) of microprojection(s)", as recited in the instant claims. In claims 29-30 of the '626 application, the step states "etching a microprojection array on said sheet member to form a plurality of microprojections", which is followed by "bending the plurality of microprojections whereby said plurality of microprojections project from a plane of said



meet member.". Thus, the etching step and bending step result in formation of microprojections, which are then coated with a drug solution. There is no step of "treating" the microprojections.

Nor is there any basis in claims 29-30 of the '626 application for asserting that it would obvious to include a "treating" step, since the claims are completely silent with respect to treatment of the microprojections. Thus, the present claims cannot be considered a mere variation of claims in the '372 patent in view of Trimmer, since one of the claims 29-30 of the '626 application. Therefore, withdrawal of the rejection for obviousness-type double patenting is respectfully requested.

**V. Conclusion**

In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 564-5887.

Respectfully submitted,

Date: Sept. 29, 06

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Michael J. Atkins  
Registration No. 35,431

Correspondence Address:  
Customer No. 27777



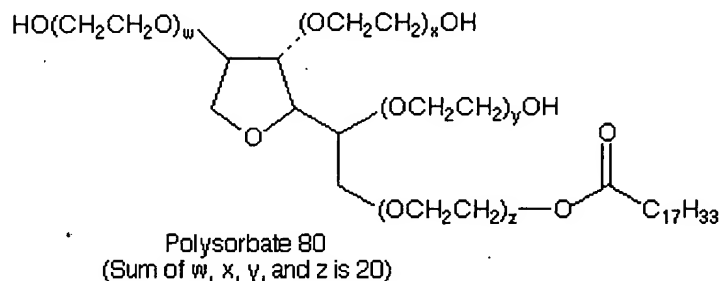


## Tween 80 by LC-MS

Tween 80 (also known as Polysorbate 80) is used in the manufacture of protein solution formulations to help solubilize and stabilize the protein. It is one of a series of materials (including Tween 20, 40 and 60) which are fatty acid esters of sorbitan polyethoxylates. The various Tweens differ in the type of fatty acid present; Tween 80 is an oleate.

Tween 80 is added into the formulation at relatively high concentrations (~0.1%), and then removed later in the manufacturing process. WCAS has developed an LC-MS method to determine the residual Tween 80 concentration down to approximately one part per million.

### Tween 80



### Testing for Tween 80

The LC separation yields a series of overlapping peaks, since Tween 80 is a mixture of isomers and congeners. Ionization is accomplished using electrospray, which gives multiply charged ions. By selecting a group of ions which correspond to a narrow band of congeners, a single chromatographic peak is obtained from the complicated Total Ion Current chromatogram (see chromatogram below).

For samples with high levels of Tween 80 (~0.05% or higher) or low salt concentrations, the samples are diluted into water and analyzed directly. For lower concentration samples, solid-phase extraction is used to separate the Tween 80 from the protein and buffer salts, which can adversely affect electrospray ionization. In either case,

accounts for any potential losses due to the preparation. This enables determination of Tween 80 from samples which originally contained high concentrations (>100 mM) of buffer salts.

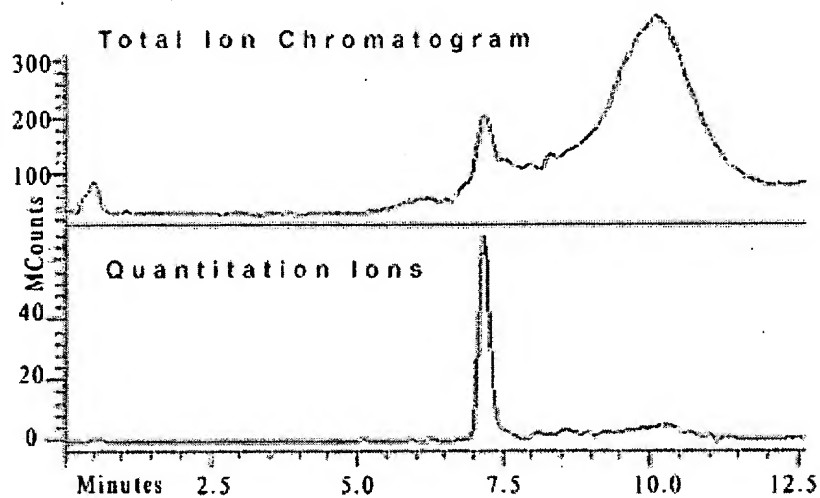
We have seen some evidence that Tween 80 from different sources can yield somewhat varying results. For that reason, it is recommended that a sample of the Tween actually used in the manufacturing process be supplied with any samples submitted for analysis. The method currently in place is applicable only to Tween 80 in the absence of other Tweens; we are investigating approaches for samples which may contain more than one.

**For more information on LC-MS**

**For a quotation...**

standards are prepared in the same manner as the samples, which

### LC-MS Chromatogram



**WCAS**

[info@wcslab.com](mailto:info@wcslab.com)

9240 Santa Fe Springs Rd  
Santa Fe Springs, CA 90670

562.948.2225 Fax 562.948.5850

**Bodycote** TESTING GROUP

PLURONIC F87 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F87 NF CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F87 NF PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F87 PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F88 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F88 PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F88 SURFACTANT PASTILLE	Consumer & Industrial :
PLURONIC F98 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F98 PRILL SURFACTANT	Consumer & Industrial :
PLURONIC L10 SURFACTANT	Consumer & Industrial :
PLURONIC L101 SURFACTANT	Consumer & Industrial :
PLURONIC L121 SURFACTANT	Consumer & Industrial :
PLURONIC L31 SURFACTANT	Consumer & Industrial :
PLURONIC L35 SURFACTANT	Consumer & Industrial :
PLURONIC L43 SURFACTANT	Consumer & Industrial :
PLURONIC L44 NF SURFACTANT	Consumer & Industrial :
PLURONIC L44 SURFACTANT	Consumer & Industrial :
PLURONIC L61 SURFACTANT	Consumer & Industrial :
PLURONIC L62 LF SURFACTANT	Consumer & Industrial :
PLURONIC L62 SURFACTANT	Consumer & Industrial :
PLURONIC L62D SURFACTANT	Consumer & Industrial :
PLURONIC L64 SURFACTANT	Consumer & Industrial :
PLURONIC L81 SURFACTANT	Consumer & Industrial :
PLURONIC L92 SURFACTANT	Consumer & Industrial :
PLURONIC N-3 SURFACTANT	Consumer & Industrial :
PLURONIC P103 SURFACTANT	Consumer & Industrial :
PLURONIC P104 SURFACTANT	Consumer & Industrial :
PLURONIC P105 SURFACTANT	Consumer & Industrial :
PLURONIC P123 SURFACTANT	Consumer & Industrial :
PLURONIC P65 SURFACTANT	Consumer & Industrial :
PLURONIC P84 SURFACTANT	Consumer & Industrial :
PLURONIC P85 SURFACTANT	Consumer & Industrial :
PLURONIC(R) F 127 MICRO PASTILLE	Consumer & Industrial :

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# Safety (MSDS) data for Tween 20

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## General

Synonyms: polyoxyethylene sorbitan monolaurate, poly(oxyethylene) sorbitan monolaurate, polyoxyethylene (20) sorbitan monolaurate, Poe 20 sorbitan monolaurate, PSML, armotan pml-20, capmul, emsorb 6915, glycospere L-20, liposorb L-20, further trade names

Use:

Molecular formula:  $C_{58}H_{114}O_{26}$

CAS No: 9005-64-5

EINECS No:

## Physical data

Appearance: liquid

Melting point:

Boiling point:

Vapour density:

Vapour pressure:

Density ( $g\ cm^{-3}$ ): 1.1

Flash point:

Explosion limits:

Autoignition temperature:

Water solubility: soluble

## Stability

Stable. Incompatible with strong oxidizing agents.

## Toxicology

Not hazardous according to directive 67/548/EC.

### Toxicity data

(The meaning of any toxicological abbreviations which appear in this section is given here.)

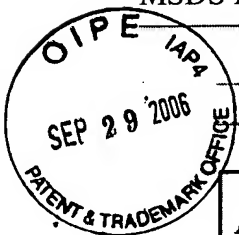
IPR-RAT LD50  $3850\ mg\ kg^{-1}$

IVN-RAT LD50  $770\ mg\ kg^{-1}$

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MSDS Number: T7683 \* \* \* \* \* Effective Date: 11/04/04 \* \* \* \* \* Supersedes: 03/28/02

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**MSDS****Material Safety Data Sheet**

From: Mallinckrodt Baker, Inc.  
222 Red School Lane  
Phillipsburg, NJ 08865



Mallinckrodt  
CHEMICALS



24 Hour Emergency Telephone: 800-850-2151  
CHEMTREC: 1-800-424-9300

National Response in Canada  
CANUTEC: 613-996-6666

Outside U.S. and Canada  
Chemtrec: 703-527-3887

**NOTE:** CHEMTREC, CANUTEC and National Response Center emergency numbers to be used only in the event of chemical emergencies involving a spill, leak, fire, exposure or accident involving chemicals.

All non-emergency questions should be directed to Customer Service (1-800-552-2537) for assistance.

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# Polysorbate 80

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## 1. Product Identification

**Synonyms:** Polyoxyethylene (20) sorbitan monooleate; Polysorbate 80 NF

**CAS No.:** 9005-65-6

**Molecular Weight:** Not applicable.

**Chemical Formula:** Not applicable.

**Product Codes:**

J.T. Baker: 2903, 4067, 4091, X257

Mallinckrodt: 7091, H286

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## 2. Composition/Information on Ingredients

Ingredient	CAS No	Percent	Hazardous
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Polysorbate 80	9005-65-6	90 - 100%	Yes

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## 3. Hazards Identification

**Emergency Overview**

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BASF Global | E-Commerce english  ContactSearch 

- **Homepage**
- **Product Information**
  - Europe
  - North America
  - Search
    - Search PlasticsPortal
    - Chemicals
    - Industries
    - ▼ Brands
    - Product Groups
    - Pharma Solutions
    - MSDS Search
    - Functional Polymers
    - Disclaimer
  - Asia Pacific
- **Services & Support**

Product Information | North America | Chemicals | **Brands****Pluronic® Surfactants**

The Pluronic® types are block copolymers based on ethylene oxide and propylene oxide. They can function as antifoaming agents, wetting agents, dispersants, thickeners, and emulsifiers. Use of the unique "Pluronic Grid" system can help a formulator decide which Pluronic® surfactant is right for his needs. The Pluronic® R types tend to generate less foam than the standard Pluronic® products, but otherwise provide similar functions.

**Products****Name****Business**

PLURONIC 10R5 SURFACTANT	Consumer & Industrial :
PLURONIC 17R2 SURFACTANT	Consumer & Industrial :
PLURONIC 17R4 SURFACTANT	Consumer & Industrial :
PLURONIC 25R2 SURFACTANT	Consumer & Industrial :
PLURONIC 25R4 SURFACTANT	Consumer & Industrial :
PLURONIC 31R1 SURFACTANT	Consumer & Industrial :
PLURONIC F108 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F108 NF CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F108 NF PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F108 PASTILLE SURFACTANT	Consumer & Industrial :
PLURONIC F108 SURFACTANT PRILL	Consumer & Industrial :
PLURONIC F127 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F127 NF 500BHT SURFACTANT PRILL	Consumer & Industrial :
PLURONIC F127 NF CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F127 NF PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F127 SURFACTANT PRILL	Consumer & Industrial :
PLURONIC F127NF 500BHT CAST SOLID SURFA	Consumer & Industrial :
PLURONIC F38 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F38 SURFACTANT PASTILLE	Consumer & Industrial :
PLURONIC F68 LF PASTILLE SURFACTANT	Consumer & Industrial :
PLURONIC F68 LF CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F68 NF CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F68 NF PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F68 PRILL SURFACTANT	Consumer & Industrial :
PLURONIC F68 SURFACTANT	Consumer & Industrial :
PLURONIC F68 SURFACTANT PASTILLE	Consumer & Industrial :
PLURONIC F77 CAST SOLID SURFACTANT	Consumer & Industrial :
PLURONIC F77 MICRO-PASTILLE SURFACTANT	Consumer & Industrial :